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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/556,937	COSTA ET AL.	
	Examiner	Art Unit	
	KAGNEW H. GEBREYESUS	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-12,17-19 and 26-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-12,17-19 and 26-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/23/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 02, 2010 has been entered.

Claims 1-15, 17-28, and 26-30 are pending. Claims 1, 8, 11, 17, 18 and 26 have been amended. Claims 29 and 30 are new. Claims 1, 8-12, 17-19, 26-30 and the elected polynucleotide species of SEQ ID NO: 5 are present for examination

All objections and rejections not reiterated from the previous Office Action are hereby withdrawn.

The following rejections were necessitated by amendment.

Claim Objections

Claim 1 is objected to because of the following informalities: On line 4-5, claim 1 recites "SEQ ID NO: 5 (sucrose non-fermenting like kinase-1; SN1LK)". However SEQ ID NO: 5 is a polynucleotide sequence. Therefore the claim must be amended to recite: "SEQ ID NO:5 (a polynucleotide that encodes sucrose non-fermenting like kinase-1; SN1LK)". Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 8-9, 11-12, 17-19, 26-29 are rejected under 35 U.S.C. 102(b) as being anticipated by US 2002/0025931 A1 (Meyers et al).

The method steps in claim 1, 8-9, 11-12, 17-19, 26-29 are drawn to an assay system that uses the polynucleotide sequence of SEQ ID NO: 5 (encodes SNF1LK) or any functional fragment that encodes a polypeptide that comprises residue 27-278 of SEQ ID NO: 5 in the presence of a candidate test agent that modulates SNF1LK and determining if the candidate test agent has an effect on the activity of the SNF1LK. In the above assay system, any agent that has an effect on the activity of the SNF1LK would be considered a candidate PTEN pathway modulating agent. Furthermore claims 29 and dependent claims thereof encompass a second assay system comprising a cell culture or non-human animals which express any MARK (see page 5, line 5-14 of the specification “MARK” encompasses a genus of kinases including the SNF1LK of SEQ ID NO: 5) in the presence of a test agent and detecting a test agent biased activity.

It should be noted that since SNF1LK is implicitly part of the PTEN pathway thus broadly interpreted, any aberrance in SNF1LK would result in aberrance in PTEN pathway thus a defective PTEN function.

Meyers et al teach a polynucleotide that encodes at least a polypeptide comprising a functionally active fragment comprising amino acid residue 27-278 of the SNF1LK of SEQ ID NO: 5 (see SEQ ID NO: 1 in fig. 1). Furthermore Meyers et al teach variants with 50%, 55%, 60%...98% identical to SEQ ID NO: 1 (this would encompass SEQ ID NO: 5 of the instant invention). The polynucleotide disclosed by Meyers et al (SEQ ID NO: 1) is 100% identical over the first 2,811 nucleotides to the polynucleotide of SEQ ID NO: 5 starting from the N-terminal. Thus the polynucleotide of SEQ ID NO: 1 encompasses at least the limitation of a polynucleotide that encodes a polypeptide comprising at least residues 27-278 of SEQ ID NO: 5 considered a functionally active fragment. In paragraph [0029], Meyers et al teach a screening method for identifying a compound that binds to or modulates the activity of a protein encoded by SEQ ID NO: 1 comprising the steps of;

-providing an indicator composition comprising an activity of a SEQ ID NO: 1 encoded protein (this can be a fragment of SEQ ID NO: 1 with kinase activity);

-providing a test compound, and determining the effect of the test compound on activity.

In addition, paragraph [0298] - [0301] Meyer et al teach a screening assays that encompasses a method for identifying modulators (i. e., candidate or test compounds or agents) which have a stimulatory or inhibitory effect on, for example, the expression or activity of the polypeptide encoded by SEQ ID NO: 1.

Thus claims 1 comprising the steps of admixing a SNF1KL or a functional fragment and an agent to be tested for its effect on the activity of said SNF1KL or

fragment thereof is clearly anticipated by Meyers et al. [It should be noted that the preamble of claim 1 in the instant application is not given patentable weight because the components and the steps in the method do not require additional components other than SNF1LK or a fragment thereof and an agent to be tested in vitro or in vivo].

Furthermore Meyers et al in paragraph [0026] teach that the agent modulates the activity or the expression of SEQ ID NO: 1 (a functionally active fragment of SEQ ID NO: 5) by modulating transcription of SEQ ID NO: 1 gene or translation of the SEQ ID NO: 1 mRNA in a cell. In yet another embodiment, they teach that the agent is a nucleic acid molecule having a nucleotide sequence that is antisense to the coding strand of a SEQ ID NO: 1 mRNA or a SEQ ID NO: 1 gene. They further teach that the antisense nucleic acid molecule can be complementary to the entire coding region of SEQ ID NO: 1 and variants mRNAs, or preferably an oligonucleotide which is antisense to only a portion of the coding or noncoding region of mRNA thus anticipating claims 8 and 9.

Furthermore as stated above since the SNF1LK (SEQ ID NO: 5 or a sequence comprising a functionally active fragment) is considered part of the pathway of PTEN, any aberrance in SNF1LK is anticipated to result in a defective PTEN function. Therefore cells comprising an aberrant expression or activity of the nucleic acid sequence of SEQ ID NO: 1 or a variant (encompasses SEQ ID NO: 5 and functionally active portion) are expected to have an aberrant PTEN function. Thus administering a wild type SNF1LK is expected to complement an aberrant SNF1LK activity. Thus wild type SNF1LK or a functionally active fragment comprising residue 27-278 of the

SNF1LK can be considered a PTEN pathway modulating agent that can restore PTEN function.

With this regard, in one embodiment, Meyers teaches a methods of using the polynucleotide of SEQ ID NO: 1 and encoded protein to treat a subject having a disorder characterized by an aberrant expression or activity of the nucleic acid sequence of SEQ ID NO: 1 or encoded protein. They state that the aberrant protein or nucleic acid expression can be characterized by a cellular growth related disorder and teach that such aberrance can be treated by administering a native protein or the nucleic acid of SEQ ID NO: 1 as a modulators.

Meyers et a also teach the use of host cells into which the expression vectors have been introduced, and non-human transgenic animals in which a sequence in which a functionally active form of SEQ ID NO: 5 (SEQ ID NO: 1) gene has been introduced or disrupted. Such host cells and transgenic non-human animals can be used in a diagnostic, screening, and therapeutic methods.

Meyers et al further teach that toxicity and therapeutic efficacy of identified compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e. g., for determining the LD50 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population) which is considered as a second assay in cells or non-human animals.

Meyers et al in paragraph [0220] that mutant polypeptide of the invention can be assayed for the ability to: 1) regulate transmission of signals from cellular receptors, e.g., cardiac cell growth factor receptors; 2) control entry of cells into mitosis; 3)

modulate cellular differentiation; 4) modulate cell death (thus apoptosis); or 5) regulate cytoskeleton function, e.g., actin bundling. Thus encompasses at least one of the embodiments in claim 28 of the instant application.

Thus claims 1, 8-9, 11-12, 17-19, 26-29 are anticipated by the disclosure of Meyers et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meyers et al in view of Summerton et al (Morpholino antisense oligomers: the case for an RNase H-independent structural type (Biochimica et Biophysica Acta 1489 (1999) 141-158) or Stein et al (A Specificity Comparison of four antisense types: Morpholino, 2'-OMethyl RNA, DNA, and Phosphorothioate DNA. Antisense & Nucleic acid Drug

Development 7:151-157 (1997). Claim 10 in the instant application teaches that the nucleic acid modulator is a phosphothioate morpholino oligomer (PMO). Claim 30 in the instant application is drawn to a nucleic acid modulator wherein said modulator is a dsRNA or an siRNA modulator.

The teachings of Meyers et al are discussed above. Briefly Meyers et al teach that the nucleic acid modulator can be an antisense oligonucleotide which can be chemically synthesized using naturally occurring nucleotides or modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed between the antisense and sense nucleic acids, e.g., phosphorothioate derivatives and acridine substituted nucleotides etc can be used. Meyers et al further teach a large number of modified nucleotides which can be used to generate the antisense nucleic acid include 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xantine etc. Furthermore they teach that the antisense nucleic acid can be produced biologically using an expression vector into which a nucleic acid has been subcloned in an antisense orientation (see paragraph [0222]).

However while Meyers et al teach a large number of modified antisense oligos including phosphorothioates as antisense oligos, they do not specifically teach using PMO oligonucleotides or dsRNA and siRNA to modulate gene expression.

Summerton et al teach that while RNase H-competent phosphorothioates (S-DNAs) have dominated the antisense field because they are reasonably resistance to nucleases, they afford good efficacy in cell-free test systems, they can be targeted

against sites throughout the RNA transcript of a gene, and their availability these merits are counterbalanced by significant limitations, including: degradation by nucleases, poor in-cell targeting predictability, low sequence specificity, and a variety of non-antisense activities. They teach that in cell-free and cultured-cell systems where one wishes to block the translation of a messenger RNA coding for a normal protein, RNase H-independent **morpholino antisense oligos** provide complete resistance to nucleases, generally good targeting predictability, generally high in-cell efficacy, excellent sequence specificity. Furthermore Stein et al teach a comparison of efficiency and specificity of four antisense types: Morpholino, 2'-OMethyl RNA, DNA, and Phosphorothioate DNA and state that Morpholino and 2'-OMethyl RNA have superior efficiency and specificity compared to the RNase H dependent antisense nucleic acids (DNA, and Phosphorothioate DNA). Therefore it would have been obvious to use RNase H-independent antisense such as PMOs to avoid the drawbacks discussed by Summerton et al. Furthermore one of ordinary skill in the art would be motivated to use any RNase H-independent antisense such as PMOs because compared to RNase dependent antisense oligos, PMOs have been shown to have higher efficiency and specificity (see Stein et al). One of ordinary skill in the art would have a reasonable expectation of success because the art clearly teaches that RNase dependent oligos and RNase independent oligos such as PMOs are known to be interchangeably used. Accordingly, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Meyers et al in view of Martinez et al. (Synthetic small inhibiting RNAs: Efficient tools to inactivate oncogenic mutations and restore p53 pathways PNAS vol. 99 no. 23 pages 14849-14854 Oct. 28, 2002).

Meyers teaching is discussed above. While Meyers et al teach antisense nucleic acid molecules to modulate transcription, they do not specifically teach siRNA or dsRNA to modulate transcription.

However at the time of the instant invention, the art was mature with regard to the use of siRNA to modulate expression of undesired genes. For example Martinez et al teach siRNAs can be used to suppress expression of point-mutated genes and state that such siRNA can provide the basis for selective and personalized anti-tumor therapy. They further teach that siRNAs have been used for various purposes and have been shown to discriminate between point mutant mRNA targets. Thus given the isolated polynucleotide sequence of SEQ ID NO: 1 (which is considered a functional variant of SEQ ID NO: 5) and the disclosure of a method of suppressing the expression of point-mutated genes it would have been obvious to specifically design an siRNA molecules to modulate/suppress expression of a polypeptide encoded by the same. One of ordinary skill in the art would be motivated to use siRNA in circumstances where it is desirable to suppress expression of aberrant forms of the polynucleotide/polypeptide of the invention. One of ordinary skill would have a reasonable expectation of success because there is no technical impediment that prevents the use of siRNA can be foreseen by a person of ordinary skill in the art.

Accordingly, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KAGNEW H. GEBREYESUS whose telephone number is (571)272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, MANJUNATH RAO can be reached on 571-272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kagnew H Gebreyesus/
Acting Examiner of Art Unit 1656
August 23, 2010